

WHAT IS CLAIMED IS:

1. A method for obtaining a prognosis for a subject having, or at risk of developing, an inflammatory condition, the method comprising determining a genotype of said subject which includes one or more polymorphic sites in the subject's thrombomodulin sequence, wherein said genotype is indicative of an ability of the subject to recover from the inflammatory condition.
2. The method of claim 1, wherein the polymorphic site is at position 5318 of SEQ ID NO:1 or at a polymorphic site in linkage disequilibrium thereto.
3. The method of claim 2, wherein the polymorphic site in linkage disequilibrium with position 5318 corresponds to position 4007 of SEQ ID NO: 1.
4. The method of claims 2 or 3, wherein the polymorphic site in linkage disequilibrium with position 5318 has a D' value of ≥ 0.8 (or r^2 value ≥ 0.8).
5. The method of any one of claims 1-4, further comprising comparing the genotype so determined with known genotypes which are known to be indicative of a prognosis for recovery from:
 - (i) the subject's type of inflammatory condition; or
 - (ii) another inflammatory condition.
6. The method any one of claims 1-5, further comprising determining the thrombomodulin sequence information for the subject.
7. The method any one of claims 1-6, wherein said determining of genotype is performed on a nucleic acid sample from the subject.
8. The method of claim 7, further comprising obtaining a nucleic acid sample from the subject.
9. The method any one of claims 1-8, wherein said determining of genotype

comprises one or more of:

- (a) restriction fragment length analysis;
- (b) sequencing;
- (c) hybridization;
- (d) oligonucleotide ligation assay;
- (e) ligation rolling circle amplification;
- (f) 5' nuclease assay;
- (g) polymerase proofreading methods;
- (h) allele specific PCR; and
- (i) reading sequence data.

10. The method of any one of claims 1-9, wherein the risk genotype of the subject is indicative of a decreased likelihood of recovery from an inflammatory condition or an increased risk of having a poor outcome.

11. The method of claim 10, wherein the subject is critically ill and the risk genotype is indicative of a prognosis of severe cardiovascular or respiratory dysfunction.

12. The method of claim 10 or 11, wherein the risk genotype comprises at least one A nucleotide at position 5318 or at least one C nucleotide at position 4007 of SEQ ID NO:1.

13. The method of any one of claims 1-9, wherein the protective genotype of the subject is indicative of an increased likelihood of recovery from an inflammatory condition.

14. The method of claim 13, wherein the subject is critically ill and the protective genotype is indicative of a prognosis of less severe cardiovascular or respiratory dysfunction.

15. The method of claim 13 or 14, wherein the protective genotype is homozygous for the C nucleotide at position 5318 or homozygous for the T nucleotide at position 4007 of SEQ ID NO:1.

16. The method of any one of claims 1-15, wherein the inflammatory condition is selected from the group consisting of: sepsis, septicemia, pneumonia, septic shock, systemic inflammatory response syndrome (SIRS), Acute Respiratory Distress Syndrome (ARDS), acute lung injury, aspiration pneumonia, infection, pancreatitis, bacteremia, peritonitis, abdominal abscess, inflammation due to trauma, inflammation due to surgery, chronic inflammatory disease, ischemia, ischemia-reperfusion injury of an organ or tissue, tissue damage due to disease, tissue damage due to chemotherapy or radiotherapy, and reactions to ingested, inhaled, infused, injected, or delivered substances, glomerulonephritis, bowel infection, opportunistic infections, and for patients undergoing major surgery or dialysis, patients who are immunocompromised, patients on immunosuppressive agents, patients with HIV/AIDS, patients with suspected endocarditis, patients with fever, patients with fever of unknown origin, patients with cystic fibrosis, patients with diabetes mellitus, patients with chronic renal failure, patients with bronchiectasis, patients with chronic obstructive lung disease, chronic bronchitis, emphysema, or asthma, patients with febrile neutropenia, patients with meningitis, patients with septic arthritis, patients with urinary tract infection, patients with necrotizing fasciitis, patients with other suspected Group A streptococcus infection, patients who have had a splenectomy, patients with recurrent or suspected enterococcus infection, other medical and surgical conditions associated with increased risk of infection, Gram positive sepsis, Gram negative sepsis, culture negative sepsis, fungal sepsis, meningococemia, post-pump syndrome, cardiac stun syndrome, stroke, congestive heart failure, hepatitis, epiglottitis, *E. coli* 0157:H7, malaria, gas gangrene, toxic shock syndrome, pre-eclampsia, eclampsia, HELP syndrome, mycobacterial tuberculosis, *Pneumocystis carinii*, pneumonia, Leishmaniasis, hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, Dengue hemorrhagic fever, pelvic inflammatory disease, Legionella, Lyme disease, Influenza A, Epstein-Barr virus, encephalitis, inflammatory diseases and autoimmunity including Rheumatoid arthritis, osteoarthritis, progressive systemic sclerosis, systemic lupus erythematosus, inflammatory bowel disease, idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, systemic vasculitis, Wegener's granulomatosis, transplants including heart, liver, lung kidney bone marrow, graft-versus-host

disease, transplant rejection, sickle cell anemia, nephrotic syndrome, toxicity of agents such as OKT3, cytokine therapy, and cirrhosis.

5 17. The method of any one of claims 1-16, wherein the inflammatory condition is SIRS.

18. A method of identifying a polymorphism in a thrombomodulin sequence that correlates with prognosis of recovery from an inflammatory condition in a subject, the method comprising:

10 (a) obtaining thrombomodulin sequence information from a group of subjects with an inflammatory condition;

(b) identifying at least one polymorphic nucleotide position in the thrombomodulin sequence in the subjects;

15 (c) determining a genotype at the polymorphic site for individual subjects in the group;

(d) determining recovery capabilities of individual subjects in the group from the inflammatory condition; and

(e) correlating genotypes determined in step (c) with the recovery capabilities determined in step (d)

20 thereby identifying said thrombomodulin polymorphisms that correlate with recovery.

25 19. The method of claim 18, wherein the inflammatory condition is selected from the group consisting of: sepsis, septicemia, pneumonia, septic shock, systemic inflammatory response syndrome (SIRS), Acute Respiratory Distress Syndrome (ARDS), acute lung injury, aspiration pneumonia, infection, pancreatitis, bacteremia, peritonitis, abdominal abscess, inflammation due to trauma, inflammation due to surgery, chronic inflammatory disease, ischemia, ischemia-reperfusion injury of an organ or tissue, tissue damage due to disease, tissue damage due to chemotherapy or radiotherapy, and reactions to ingested, inhaled, 30 infused, injected, or delivered substances, glomerulonephritis, bowel infection,

opportunistic infections, and for subjects undergoing major surgery or dialysis,
 subjects who are immunocompromised, subjects on immunosuppressive agents,
 subjects with HIV/AIDS, subjects with suspected endocarditis, subjects with fever,
 subjects with fever of unknown origin, subjects with cystic fibrosis, subjects with
 5 diabetes mellitus, subjects with chronic renal failure, subjects with bronchiectasis,
 subjects with chronic obstructive lung disease, chronic bronchitis, emphysema, or
 asthma, subjects with febrile neutropenia, subjects with meningitis, subjects with
 septic arthritis, subjects with urinary tract infection, subjects with necrotizing
 fasciitis, subjects with other suspected Group A streptococcus infection, subjects
 10 who have had a splenectomy, subjects with recurrent or suspected enterococcus
 infection, other medical and surgical conditions associated with increased risk of
 infection, Gram positive sepsis, Gram negative sepsis, culture negative sepsis,
 fungal sepsis, meningococemia, post-pump syndrome, cardiac stun syndrome,
 stroke, congestive heart failure, hepatitis, epiglottitis, *E. coli* 0157:H7, malaria, gas
 15 gangrene, toxic shock syndrome, pre-eclampsia, eclampsia, HELP Syndrome,
 mycobacterial tuberculosis, *Pneumocystis carinii*, pneumonia, Leishmaniasis,
 hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, Dengue
 hemorrhagic fever, pelvic inflammatory disease, Legionella, Lyme disease,
 Influenza A, Epstein-Barr virus, encephalitis, inflammatory diseases and
 20 autoimmunity including Rheumatoid arthritis, osteoarthritis, progressive systemic
 sclerosis, systemic lupus erythematosus, inflammatory bowel disease, idiopathic
 pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, systemic vasculitis,
 Wegener's granulomatosis, transplants including heart, liver, lung kidney bone
 marrow, graft-versus-host disease, transplant rejection, sickle cell anemia,
 25 nephrotic syndrome, toxicity of agents such as OKT3, cytokine therapy, and
 cirrhosis.

20. A kit for determining a genotype at a defined nucleotide position within a
 polymorphic site in a thrombomodulin sequence, wherein knowledge of the
 30 genotype provides a prognosis of the subject's ability to recover from an
 inflammatory condition, the kit comprising;
 - (a) a restriction enzyme capable of distinguishing alternate nucleotides at the
 polymorphic site; or

- (b) a labeled oligonucleotide that is sufficiently complementary to an alternate nucleotide sequence at the polymorphic site so as to be capable of specifically hybridizing to said alternate nucleotide sequence, whereby the genotype of the polymorphic site may be determined; and
- 5 (c) optionally, instructions for use in determining the genotype.

21. The kit of claim 20, wherein a polymorphism site corresponds to position 5318 or position 4007 of SEQ ID NO:1.

10 22. The kit of claim 20 or 21 further comprising an oligonucleotide or a set of oligonucleotides suitable to amplify a region including the polymorphic site.

23. The kit of claim 22, further comprising a polymerizing agent.

15 24. A method for selecting a group of subjects for determining the efficacy of a candidate drug known or suspected of being useful for the treatment of an inflammatory condition, the method comprising determining a genotype for one or more polymorphic sites in the thrombomodulin sequence for each subject, wherein said genotype is indicative of the subject's ability to recover from the
20 inflammatory condition and sorting subjects based on their genotype.

25. The method of claim 24 further comprising, administering the candidate drug to the subjects or a subset of subjects and determining each subject's ability to recover from the inflammatory condition.

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26. The method of claim 25, further comprising comparing subject response to the candidate drug based on genotype of the subject.

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27. An oligonucleotide of about 10 to about 400 nucleotides that hybridizes specifically to a sequence contained in a *human* target sequence consisting of SEQ ID NO:1, a complementary sequence of the target sequence or RNA equivalent of the target sequence and wherein the oligonucleotide is operable in determining a polymorphism genotype.

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29. An oligonucleotide probe selected from the group consisting of:

- (a) a probe that hybridizes under high stringency conditions to a nucleic acid molecule comprising SEQ ID NO:1 having a A at position 5318 but not to a nucleic acid molecule comprising SEQ ID NO:1 having a C at position 5318;
- (b) a probe that hybridizes under high stringency conditions to a nucleic acid molecule comprising SEQ ID NO:1 having a C at position 5318 but not to a nucleic acid molecule comprising SEQ ID NO:1 having a A at position 5318;
- (c) a probe that hybridizes under high stringency conditions to a nucleic acid molecule comprising SEQ ID NO:1 having a C at position 4007 but not to a nucleic acid molecule comprising SEQ ID NO:1 having a T at position 4007; and
- (d) a probe that hybridizes under high stringency conditions to a nucleic acid molecule comprising SEQ ID NO:1 having a T at position 4007 but not to a nucleic acid molecule comprising SEQ ID NO:1 having a C at position 4007.

30. An array of nucleic acid molecules attached to a solid support, the array comprising an oligonucleotide that will hybridize to a nucleic acid molecule consisting of SEQ ID NO:1, wherein the nucleotide at position 5318 is A, under conditions in which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 wherein the nucleotide at position 5318 is C.

31. An array of nucleic acid molecules attached to a solid support, the array comprising an oligonucleotide that will hybridize to a nucleic acid molecule consisting of SEQ ID NO:1, wherein the nucleotide at position 5318 is C, under conditions in which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 wherein the nucleotide at position 5318 is A.

32. An array of nucleic acid molecules attached to a solid support, the array comprising an oligonucleotide that will hybridize to a nucleic acid molecule consisting of SEQ ID NO:1, wherein the nucleotide at position 4007 is C, under conditions in which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 wherein the nucleotide at position 4007 is T.
33. An array of nucleic acid molecules attached to a solid support, the array comprising an oligonucleotide that will hybridize to a nucleic acid molecule consisting of SEQ ID NO:1, wherein the nucleotide at position 4007 is T, under conditions in which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting of SEQ ID NO:1 wherein the nucleotide at position 4007 is C.
34. An oligonucleotide of any one of claims 27 to 33, further comprising one or more of the following: a detectable label; a quencher; a mobility modifier; a contiguous non-target sequence situated 5' or 3' to the target sequence.
35. A computer readable medium comprising a plurality of digitally encoded genotype correlations selected from the thrombomodulin genotype correlations in TABLE 2B, wherein each correlation of the plurality has a value representing an ability to recover from an inflammatory condition.